

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Withdrawn) A method for sterilizing a preparation of one or more digestive enzymes that is sensitive to radiation, said method comprising irradiating said preparation of one or more digestive enzymes with radiation for a time effective to sterilize said preparation of one or more digestive enzymes at a rate effective to sterilize said preparation of one or more digestive enzymes and to protect said preparation of one or more digestive enzymes from said radiation.

2. (Withdrawn) A method for sterilizing a preparation of one or more digestive enzymes that is sensitive to radiation, said method comprising:

(i) adding to said preparation of one or more digestive enzymes at least one stabilizer in an amount effective to protect said preparation of one or more digestive enzymes from said radiation; and

(ii) irradiating said preparation of one or more digestive enzymes with a suitable radiation at an effective rate for a time effective to sterilize said preparation of one or more digestive enzymes.

3. (Withdrawn) A method for sterilizing a preparation of one or more digestive enzymes that is sensitive to radiation, said method comprising:

(i) reducing the residual solvent content of said preparation of one or more digestive enzymes to a level effective to protect said preparation of one or more digestive enzymes from said radiation; and

(ii) irradiating said preparation of one or more digestive enzymes with a suitable radiation at an effective rate for a time effective to sterilize said preparation of one or more digestive enzymes.

4. (Withdrawn) A method for sterilizing a preparation of one or more digestive enzymes that is sensitive to radiation, said method comprising:

(i) reducing the temperature of said preparation of one or more digestive enzymes to a level effective to protect said preparation of one or more digestive enzymes from said radiation; and

(ii) irradiating said preparation of one or more digestive enzymes with a suitable radiation at an effective rate for a time effective to sterilize said preparation of one or more digestive enzymes.

5. (Currently Amended) A method for sterilizing a preparation of one or more digestive enzymes that is sensitive to radiation, said method comprising:

(i) applying to said preparation of one or more digestive enzymes prior to irradiating at least one a stabilizing process selected from the group consisting of

(a) ~~reducing the residual solvent content of said preparation of one or more digestive enzymes;~~

(b) ~~reducing the temperature of said preparation of one or more digestive enzymes~~ below ambient temperature; and

(c) ~~adding at least one stabilizer to said preparation of one or more digestive enzymes; and~~

(ii) irradiating said preparation of one or more digestive enzymes with a suitable radiation at an effective rate for a time effective to sterilize said preparation of one or more digestive enzymes, wherein said ~~at least one~~ stabilizing process and the rate of irradiation are together effective to protect said preparation of one or more digestive enzymes from said radiation.

6. (Currently Amended) The method according to claim 5, ~~wherein said applying to said preparation of one or more digestive enzymes at least one stabilizing process further comprising~~ comprises applying to said preparation of one or more digestive enzymes prior to

irradiating at least ~~two processes~~ one additional stabilizing process selected from the group consisting of: (a) reducing the residual solvent content of said preparation of one or more digestive enzymes; and (b) adding at least one stabilizer to said preparation of one or more digestive enzymes, wherein said ~~at least two~~ stabilizing processes are together effective to protect said preparation of one or more digestive enzymes from said radiation and further wherein said ~~at least two~~ stabilizing processes may be performed in any order.

7. (Currently Amended) The method according to claim 5 or 6, further comprising reducing the residual solvent content of said preparation of one or more digestive enzymes prior to irradiating, wherein said solvent is water.

8. (Original) The method according to claim 7, wherein said residual water content is reduced by the addition of an organic solvent.

9. (Currently Amended) The method according to claim 5 or 6, further comprising reducing the residual solvent content of said preparation of one or more digestive enzymes prior to irradiating, wherein said solvent is an organic solvent.

10. (Currently Amended) The method according to claim 5 or 6, wherein said preparation of one or more digestive enzymes is suspended in an organic solvent following reduction of ~~[[said]]~~ a residual solvent content.

11. (Currently Amended) The method according to claim 5 or 6, wherein said effective rate is not more than ~~about~~ 3.0 kGy/hour.

12. (Currently Amended) The method according to claim 5 or 6, wherein said effective rate is not more than ~~about~~ 2.0 kGy/hr.

13. (Currently Amended) The method according to claim 5 or 6, wherein said effective rate is not more than ~~about~~ 1.0 kGy/hr.

14. (Currently Amended) The method according to claim 5 or 6, wherein said effective rate is not more than ~~about~~ 0.3 kGy/hr.

15. (Currently Amended) The method according to claim 5 or 6, wherein said effective rate is more than ~~about~~ 3.0 kGy/hour.

16. (Currently Amended) The method according to claim 5 or 6, wherein said effective rate is at least ~~about~~ 6.0 kGy/hour.

17. (Currently Amended) The method according to claim 5 or 6, wherein said effective rate is at least ~~about~~ 18.0 kGy/hour.

18. (Currently Amended) The method according to claim 5 or 6, wherein said effective rate is at least ~~about~~ 30.0 kGy/hour.

19. (Currently Amended) The method according to claim 5 or 6, wherein said effective rate is at least ~~about~~ 45 kGy/hour.

20. (Previously Presented) The method according to claim 5 or 6, wherein said preparation of one or more digestive enzymes is maintained in a low oxygen atmosphere.

21. (Previously Presented) The method according to claim 5 or 6, wherein said preparation of one or more digestive enzymes is maintained in an atmosphere comprising at least one noble gas.

22. (Original) The method according to claim 21, wherein said noble gas is argon.

23. (Previously Presented) The method according to claim 5 or 6, wherein said preparation of one or more digestive enzymes is maintained in a vacuum.

24. (Currently Amended) The method according to claim 5 or 6, further comprising reducing the residual solvent content of said preparation of one or more digestive enzymes prior to irradiating, wherein said residual solvent content is reduced by a method selected from the group consisting of lyophilization, drying, concentration, addition of solute, evaporation, chemical extraction, spray-drying, ~~and vitrification~~ and combinations of two or more thereof.

25. (Currently Amended) The method according to claim 5 or 6, further comprising reducing the residual solvent content of said preparation of one or more digestive enzymes prior to irradiating, wherein said residual solvent content is less than ~~about~~ 15%.

26. (Currently Amended) The method according to claim 5 or 6, further comprising reducing the residual solvent content of said preparation of one or more digestive enzymes prior to irradiating, wherein said residual solvent content is less than ~~about~~ 10%.

27. (Currently Amended) The method according to claim 5 or 6, further comprising reducing the residual solvent content of said preparation of one or more digestive enzymes prior to irradiating, wherein said residual solvent content is less than ~~about~~ 3%.

28. (Currently Amended) The method according to claim 5 or 6, further comprising reducing the residual solvent content of said preparation of one or more digestive enzymes prior to irradiating, wherein said residual solvent content is less than ~~about~~ 2%.

29. (Currently Amended) The method according to claim 5 or 6, further comprising reducing the residual solvent content of said preparation of one or more digestive enzymes prior to irradiating, wherein said residual solvent content is less than ~~about~~ 1%.

30. (Currently Amended) The method according to claim 5 or 6, further comprising reducing the residual solvent content of said preparation of one or more digestive enzymes prior to irradiating, wherein said residual solvent content is less than ~~about~~ 0.5%.

31. (Currently Amended) The method according to claim 5 or 6, further comprising reducing the residual solvent content of said preparation of one or more digestive enzymes prior to irradiating wherein said residual solvent content is less than about 0.08%.

32. (Previously Presented) The method according to claim 5 or 6, wherein at least one sensitizer is added to said preparation of one or more digestive enzymes prior to said step of irradiating said preparation of one or more digestive enzymes.

33. (Previously Presented) The method according to claim 5 or 6, wherein said preparation of one or more digestive enzymes contains at least one biological contaminant or pathogen selected from the group consisting of viruses, bacteria, yeasts, molds, fungi, prions or similar agents responsible, alone or in combination, for TSEs and single or multicellular parasites.

34. (Currently Amended) The method according to claim 5 or 6, further comprising adding an effective amount of at least one stabilizer to said preparation of one or more digestive enzymes prior to irradiating, wherein said at least one stabilizer ~~is~~ comprises an antioxidant.

35. (Currently Amended) The method according to claim 5 or 6, further comprising adding an effective amount of least one stabilizer to said preparation of one or more digestive enzymes prior to irradiating, wherein said at least one stabilizer ~~is~~ comprises a free radical scavenger.

36. (Currently Amended) The method according to claim 5 or 6, further comprising adding an effective amount of least one stabilizer to said preparation of one or more digestive enzymes prior to irradiating, wherein said at least one stabilizer is a combination stabilizer.

37. (Currently Amended) The method according to claim 5 or 6, further comprising adding an effective amount of least one stabilizer to said preparation of one or more digestive enzymes prior to irradiating, wherein said at least one stabilizer ~~is~~ comprises a ligand.

38. (Original) The method according to claim 37, wherein said ligand is heparin.

39. (Currently Amended) The method according to claim 5 or 6, further comprising adding an effective amount of least one stabilizer to said preparation of one or more digestive enzymes prior to irradiating, wherein said at least one stabilizer reduces damage due to reactive oxygen species.

40. (Currently Amended) The method according to claim 5 or 6, further comprising adding an effective amount of least one stabilizer to said preparation of one or more digestive enzymes prior to irradiating, wherein said at least one stabilizer is selected from the group consisting of: ascorbic acid or a salt or ester thereof; glutathione; 6-hydroxy-2,5,7,8-

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tetramethylchroman-2-carboxylic acid; uric acid or a salt or ester thereof; methionine; histidine; N-acetyl cysteine; lipoic acid; sodium formaldehyde sulfoxylate; gallic acid or a derivative thereof; propyl gallate and mixtures of two or more thereof.

41. (Currently Amended) The method according to claim 40, wherein said mixtures of two or more additional stabilizers are selected from the group consisting of: mixtures of ascorbic acid, or a salt or ester thereof, and uric acid, or a salt or ester thereof; mixtures of ascorbic acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; and mixtures of uric acid, or a salt or ester thereof, lipoic acid, sodium formaldehyde sulfoxylate, gallic acid or a derivative thereof, propyl gallate and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid.

42. (Currently Amended) The method according to claim 5 or 6, further comprising adding an effective amount of at least one stabilizer to said preparation of one or more digestive enzymes prior to irradiating, wherein said at least one stabilizer is a dipeptide stabilizer.

43. (Currently Amended) The method according to claim 42, wherein said dipeptide stabilizer is selected from the group consisting of glycyl-glycine (Gly-Gly), carnosine, ~~and~~ anserine and combinations of two or more thereof.

44. (Previously Presented) The method according to claim 5 or 6, wherein said radiation is corpuscular radiation or electromagnetic radiation, or a mixture thereof.

45. (Original) The method according to claim 44, wherein said electromagnetic radiation is selected from the group consisting of radio waves, microwaves, visible and invisible light, ultraviolet light, x-ray radiation, gamma radiation and combinations thereof.

46. (Currently Amended) The method according to claims [[1, 2, 3, 4,]] 5 or 6, wherein said radiation is gamma radiation.

47. (Previously Presented) The method according to claim 5 or 6, wherein said radiation is E-beam radiation.

48. (Previously Presented) The method according to claim 5 or 6, wherein said radiation is visible light.

49. (Previously Presented) The method according to claim 5 or 6, wherein said radiation is ultraviolet light.

50. (Previously Presented) The method according to claim 5 or 6, wherein said radiation is x-ray radiation.

51. (Previously Presented) The method according to claim 5 or 6, wherein said radiation is polychromatic visible light.

52. (Previously Presented) The method according to claim 5 or 6, wherein said radiation is infrared.

53. (Previously Presented) The method according to claim 5 or 6, wherein said radiation is a combination of one or more wavelengths of visible and ultraviolet light.

54. (Cancelled)

55. (Previously Presented) The method according to claim 5 or 6, wherein said irradiation is conducted at a temperature below ambient temperature.

56. (Previously Presented) The method according to claim 5 or 6, wherein said irradiation is conducted below the freezing point of said preparation of one or more digestive enzymes.

57. (Previously Presented) The method according to claim 5 or 6, wherein said irradiation is conducted below the eutectic point of said preparation of one or more digestive enzymes.

58. (Cancelled).

59. (Withdrawn) A composition comprising at least one preparation of one or more digestive enzymes and at least one stabilizer in an amount effective to preserve said preparation of one or more digestive enzymes for its intended use following sterilization with radiation.

60. (Withdrawn) A composition comprising at least one preparation of one or more digestive enzymes, wherein the residual solvent content of said preparation of one or more digestive enzymes is at a level effective to preserve said preparation of one or more digestive enzymes for its intended use following sterilization with radiation.

61. (Withdrawn) The composition of claim 60, wherein said residual solvent content is less than ~~about~~ 15%.

62. (Withdrawn) The composition of claim 60, wherein said residual solvent content is less than ~~about~~ 10%.

63. (Withdrawn) The composition of claim 60, wherein said residual solvent content is less than ~~about~~ 5%.

64. (Withdrawn) The composition of claim 60, wherein said residual solvent content is less than ~~about~~ 2%.

65. (Withdrawn) The composition of claim 60, wherein said residual solvent content is less than ~~about~~ 1%.

66. (Withdrawn) The composition of claim 60, wherein said residual solvent content is less than ~~about~~ 0.5%.

67. (Withdrawn) The composition of claim 60, wherein said residual solvent content is less than ~~about~~ 0.08%.

68. (Withdrawn) The composition of claim 59 or 60, wherein said preparation of one or more digestive enzymes is glassy or vitrified.

69. (Withdrawn) The composition of claim 59 or 60, wherein said preparation of one or more digestive enzymes contains at least one enzyme selected from the group consisting of trypsin, glycosidases and sulfatases.

70. (Withdrawn) The composition of claim 60, wherein the total protein concentration of said preparation of one or more digestive enzymes is at least ~~about~~ 0.5%.

71. (Withdrawn) The composition of claim 60, wherein the total protein concentration of said preparation of one or more digestive enzymes is at least ~~about~~ 1%.

72. (Withdrawn) The composition of claim 60, wherein the total protein concentration of said preparation of one or more digestive enzymes is at least ~~about~~ 5%.

73. (Withdrawn) The composition of claim 60, wherein the total protein concentration of said preparation of one or more digestive enzymes is at least ~~about~~ 10%.

74. (Withdrawn) The composition of claim 60, wherein the total protein concentration of said preparation of one or more digestive enzymes is at least ~~about~~ 15%.

75. (Withdrawn) The composition of claim 60, wherein the total protein concentration of said preparation of one or more digestive enzymes is at least ~~about~~ 20%.

76. (Withdrawn) The composition of claim 60, wherein the total protein concentration of said preparation of one or more digestive enzymes is at least ~~about~~ 25%.

77. (Withdrawn) The composition of claim 60, wherein the total protein concentration of said preparation of one or more digestive enzymes is at least ~~about~~ 50%.

78. (Withdrawn) A method of treating a digestive enzyme deficiency in a mammal comprising administering to a mammal in need thereof an effective amount of a preparation of one or more digestive enzymes which has been sterilized according to the method according to claim 1, 2, 3, 4, 5 or 6.

79. (Withdrawn) The method according to claim 78, wherein said mammal is a human.

80. (Withdrawn) The method according to claim 78, wherein said digestive enzyme deficiency is Fabry disease.

81. (Withdrawn) The method according to claim 78, wherein said digestive enzyme deficiency is Hunter syndrome.

82. (Withdrawn) The method according to claim 78, wherein said digestive enzyme deficiency is Gaucher's disease.

83. (Withdrawn) The method according to claim 78, wherein said preparation of one or more digestive enzymes comprises α -galactosidase.

84. (Withdrawn) The method according to claim 78, wherein said preparation of one or more digestive enzymes comprises iduronate-2-sulfatase.

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85. (Withdrawn) The method according to claim 37, wherein said ligand is a substrate or substrate analog of at least one digestive enzyme contained in said preparation of one or more digestive enzymes.

86. (New) The method according to claim 5 or 6, further comprising adding an effective amount of at least one stabilizer to said preparation of one or more digestive enzymes prior to irradiating.